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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/674,035	12/11/2000	Jas C. Lang	22727/04078	9153

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EXAMINER	
HELMS, LARRY RONALD	
ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 06/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/674,035	LANG, JAS C.	
	Examiner	Art Unit	
	Larry R. Helms	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5 and 9-21* is/are pending in the application.

4a) Of the above claim(s) *10-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,9 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 1 in part and claims 2-5, 9, 21 in Paper filed 4/25/02 is acknowledged. Claim 1 will be examined that the method detects a nucleic acid molecule.

2. Claims 10-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions. Election was made **without** traverse in Paper filed 4/25/02.

Claim Objections

3. Claim 1 is objected to because of the following informalities: Claims 1 encompasses non-elected inventions in that the method uses an antibody, see restriction requirement of Group II.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 3 is indefinite for reciting "mature form of the DESC1 protein comprises" amino acids of SEQ ID NO:2 or 4 and "soluble form of DESC 1 protein comprises" 191-422 of SEQ ID NO:2 or 4 because it is unclear if the soluble form is the mature form because the soluble form "comprises 191-422" and as such can encompass the mature form. What is the difference between the mature and the soluble form?

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claims 4-5 are rejected under 35 U.S.C. ' 101 because the claimed invention is directed to non-statutory subject matter.

Claims 4-5, as written, do not sufficiently distinguish over vectors and host cells as they exists naturally because claims do not particularly point out any non-naturally occurring differences between the claimed vectors and host cells and the structure of naturally occurring vectors and host cells if transformed by viral vectors as contemplated in the specification on page 5.

In the absence of the hand of man, the naturally occurring antibodies are considered non-statutory subject matter (Diamond v. Chakrabarty, 206 U.S.P.Q. 193 (1980)). It should be noted that the mere purity of a naturally occurring product does

not necessarily impart patentability (Ex parte Siddiqui, 156 U.S.P.Q. 426 (1966)). However, when purification results in a new utility, patentability is considered (Merck Co. v. Chase Chemical Co., 273 F.Supp 68 (1967), 155 USPQ 139, (District Court, New Jersey, 1967)). Amendment of the claims to recite "an isolated" or "purified" recombinant vector or recombinant host cell or similar language would obviate this rejection.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-2, 4-5, 9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 1 and 9 recite "DESC1" gene or protein and claim 2 recites a protein having 90% identity to SEQ ID NO:2 or 4. The specification teaches only a DESC1 protein of SEQ ID NO:2 or 4 and a cDNA of SEQ ID NO:1 and 3. The term DESC1 protein encompasses variants (see page 7) and the specification does not teach any such variants or genes as broadly encompassed by the claims.

The general knowledge in the art concerning variants does not provide any indication of how the structure of one variant is representative of unknown variants. Reiger et al. (Glossary of Genetics and Cytogenetics, Classical and Molecular, 4th Ed., Springer-Verlay, Berlin, 1976) clearly define alleles as one of two or more alternative forms of a gene occupying the same locus on a particular chromosome... and differing from other alleles of that locus at one or more mutational sites (page 17). Thus, the structure of naturally occurring allelic sequences are not defined. With the exception of SEQ ID NO:2 the skilled artisan cannot envision the detailed structure of the encompassed polypeptides and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation.

The claims are drawn to a "gene", however, according to Genes IV (Lewin et al, Oxford University Press, page 810, 1990), a gene is defined as "the segment of DNA involved in producing a polypeptide chain; it includes regions preceding and following the coding regions (leader and trailer) as well as intervening sequences (introns) between individual coding segments (exons)." From the teachings of the specification, however, the nucleic acid sequences appear limited to the specific coding regions, and do not include expression control elements that fall under the definition of a gene.

Thus, one of skill in the art would not understand that the applicant had possession of the claimed invention at the time the instant application was filed.

9. Claims 1-2, 4-5, 9, 21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of detecting the expression of SEQ ID NO:1 or 3 with a nucleotide probe and a nucleic acid that encodes SEQ ID NO:2 or 4 or a nucleic acid of SEQ ID NO:1 and 3 and a vector and host cell comprising such, does not reasonably provide enablement for a method of detecting just any DESC1 expression, a nucleic acid that encodes a protein that is 90% identical to SEQ ID NO:2 or 4 or vectors and host cell comprising such or a nucleic acid that encodes a mature form of DESC1 and hybridizes to SEQ ID NO:1 or 3 or a nucleic acid that hybridizes under stringent conditions to 626-1321 of SEQ ID NO:1 or 3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The claims are broadly drawn to detecting the expression of an y DESC1 gene or an isolated nucleic acid that encodes a protein that is 90% identical to SEQ ID NO:2 or 4 or encodes a mature form that hybridizes to SEQ ID NO:1 or 3 or nucleotides 626-1321 of SEQ ID NO:1 or 3. The specification discloses that SEQ ID NO:1 or 3 are not

expressed in carcinomas and expressed in normal tissue (see page 15 and Figure 3A). The specification discloses that SEQ ID NO:2 or 4 are the DESC1 protein. The specification does not teach a function for DESC1 but contemplates that it is homologous, 38% overall, with the HAT protein and predict a catalytic domain (see page 6-7). The claims do not require a function and as such alterations in the protein sequence can lead to alteration in protein function.

Protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, the replacement of a single lysine at position 118 of the acidic fibroblast growth factor by a glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological activity of the protein (see Burgess et al, Journal of Cell Biology Vol 111 November 1990 2129-2138). In transforming growth factor alpha, replacement of aspartic acid at position 47 with asparagine, did not affect biological activity while the replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen (see Lazar et al Molecular and Cellular Biology Mar 1988 Vol 8 No 3 1247-1252).

Replacement of the histidine at position 10 of the B-chain of human insulin with aspartic acid converts the molecule into a superagonist with 5 times the activity of nature human insulin. Schwartz et al, Proc Natl Acad Sci USA Vol 84:6408-6411 (1987). Removal of the amino terminal histidine of glucagon substantially decreases the ability of the molecule to bind to its receptor and activate adenylate cyclase. Lin et al Biochemistry USA Vol 14:1559-1563 (1975).

These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of the protein.

The claims encompass any nucleic acid that hybridizes under stringent conditions to SEQ ID NO:1 or 3 but the nucleic acid does not have to encode SEQ ID NO:2 or 4 it has to encode a "mature" form. The specification discloses many stringent conditions on pages 3-4 and as such one skill in the art would not know what conditions to use to get the required hybridization. In addition, the specification only discloses SEQ ID NO:2 or 4 as a mature form. All nucleic acids that would hybridize under the recited conditions would not encode a "mature DESC1" protein as required in the claims or be differentially expressed in tumor tissue as in SEQ ID NO:1 and 3. In addition all nucleic acids that hybridize would not be used to determine the expression of the DESC1 nucleic acid and as such one would not know how to use such nucleic acids.

In view of the lack of guidance, lack of examples, and lack of predictability in the art as evidenced from the above discussion, one skilled in the art would be forced into undue experimentation in order to practice the broadly claimed invention.

Priority

10. The description of SEQ ID NO:3 and 4 are not seen in provisional application 60/122,747. Therefore claims 2-4, 9, 21 are granted the priority date of 11/99 where in PCT/IB99/01818 describes SEQ ID NO:1-4.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1-5, 9, 21 are rejected under 35 U.S.C. 102(e) as being anticipated by Baker et al (US patent application publication US 2003/0073129, with priority to at least 10/98).

The claims recite a method of detecting DESC1 expression and a nucleic acid that encodes a protein that is at least 90% identical to SEQ ID NO:2 or 4 and a nucleic acid that encodes SEQ ID NO:2 or 4 , and vectors and host cells and a nucleic acid that encodes the mature form of DESC1 which hybridizes to SEQ ID NO:1 or 3 and hybridizes to 626-1321 of SEQ ID NO:1 or 3.

Baker et al teach the exact amino acid sequence of SEQ ID NO:2 (See SEQ ID NO:269 and PRO 1461) and the exact nucleic acid of SEQ ID NO:1 (See SEQ ID NO:268). Baker also teach methods of detecting expression with nucleic acid probes (see page 210) and vectors and host cells (see page 210). Baker et al's SEQ ID NO:1 would hybridize under the recited conditions to SEQ ID NO:3 because the nucleic acids are highly homologous (see attached alignment on back of Office Action). Because Baker et al's amino acid sequence is identical to SEQ ID NO:2 and only differs at positions 24, 37, 391 of SEQ ID NO:4 and Baker et al's sequence would be the "mature" form of the protein.

13. Claim 21 is rejected under 35 U.S.C. 102(b) as being anticipated by The 1991 Boehringer Mannheim Biochemical Catalog, page 557.

The claim recites a nucleic acid that hybridizes under stringent conditions to 626-1321 of SEQ ID NO:1 or 3.

The Boehringer Mannheim Biochemical Catalog, page 557 teach random primers that would hybridize under the recited condition to the recited sequence.

Conclusion

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (571)

272-0832. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ~~Christina Chan~~ JEFFREY SIEW, can be reached at (571) 272-~~0841~~ 0787.

16. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center telephone number is 703-872-9306.

Respectively,

Larry R. Helms

571-272-0832

LARRY R. HELMS, PH.D
PRIMARY EXAMINER